

Ab Initio Molecular Orbital Study of Energies and Conformers of 3,4-Dihydro-1,2-Dithiin, 3,6-Dihydro-1,2-Dithiin, 4*H*-1,3-Dithiin, and 2,3-Dihydro-1,4-Dithiin

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Received 25 February 1997; accepted 16 February 1998

ABSTRACT: Optimized geometries and energies for 3,4-dihydro-1,2-dithiin (1), 3,6-dihydro-1,2-dithiin (2), 4*H*-1,3-dithiin (3), and 2,3-dihydro-1,4-dithiin (4) were calculated using *ab initio* 6-31G* and MP2/6-31G*//6-31G* methods. At the MP2/6-31G*//6-31G* level, the half-chair conformer of 4 is more stable than those of 1, 2, and 3 by 2.5, 3.5, and 3.6 kcal/mol, respectively. The half-chair conformers of 1, 2, 3, and 4 are 2.9, 7.1, 2.0, and 5.6 kcal/mol, respectively, more stable than their boat conformers. The calculated half-chair structures of 1–4 are compared with the calculated chair conformer of cyclohexane and the half-chair structures for cyclohexene, 3,4-dihydro-1,2-dioxin (5), 3,6-dihydro-1,2-dioxin (6), 4*H*-1,3-dioxin (7), and 2,3-dihydro-1,4-dioxin (8). © 1998 John Wiley & Sons, Inc. J Comput Chem 19: 1064–1071, 1998

Keywords: anomeric effects; boat conformers, dihydrodioxins; 3,4-dihydro-1,2-dithiin; 3,6-dihydro-1,2-dithiin; 4*H*-1,3-dithiin; 2,3-dihydro-1,4-dithiin; dihydrodithiins; half-chair conformers; hyperconjugative orbital interactions; relative energies; stereoelectronic effects

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Contract/grant sponsor: National Science Foundation; contract/grant numbers: CHE-9015849, CHE-9311713

This article includes Supplementary Material available from the authors upon request or via the Internet at <ftp.wiley.com/public/journals/jcc/suppmat/19/1064> or <http://journals.wiley.com/jcc/>

Introduction

The addition of a double bond and the replacement of carbon by another element in cycloalkanes will produce changes in several structural parameters and, consequently, will affect the conformational characteristics of the molecules. For example, introduction of a double bond and a nitrogen, an oxygen, or a sulfur atom for carbon in cyclohexane will lead to a change in bond lengths (C—C 1.54 Å, C=C 1.34 Å, C—N 1.47 Å, C—O 1.43 Å, C—S 1.82 Å) and bond angles. Introduction of a second heteroatom into these unsaturated heterocycles will bring about additional significant structural and conformational changes.

Among the factors that will primarily determine the relative stability of the conformers of six-membered unsaturated heterocycles, such as 3,4-dihydro-1,2-dithiin (1),^{1–3} 3,6-dihydro-1,2-dithiin (2),^{2–4} 4H-1,3-dithiin (3),³ 2,3-dihydro-1,4-dithiin (4),^{5–7} 3,4-dihydro-1,2-dioxin (5),⁸ 3,6-dihydro-1,2-dioxin (6),^{4,8} 4H-1,3-dioxin (7),⁸ and 2,3-dihydro-1,4-dioxin (8),⁸ are angle strain, lone pair-lone pair repulsion, π electron-lone pair repulsion, and torsional strain resulting from eclipsing of adjacent methylene groups. Information concerning the conformations and structural properties of unsaturated sulfur heterocycles 1–4 and their derivatives is of considerable interest owing to their unique molecular properties,^{4–6} to their bioactivity,^{2,3} and to their occurrence in natural products.^{2,3} A computational study of dihydrodithiins 1–4 is especially important since the report of possible hyperconjugative orbital interactions (anomeric effects) in 4H-1,3-dioxin 7 ($n_{O(3)} \rightarrow \sigma_{C(2)-O(1)}^*$, $n_{O(3)} \rightarrow \sigma_{C(2)-H_{ax}}^*$ and $n_{O(1)} \rightarrow \sigma_{C(2)-H_{ax}}^*$) and in 2,3-dihydro-1,4-dioxin 8 ($n_O \rightarrow \sigma_{C-H_{ax}}^*$).⁸



The hyperconjugative orbital interactions (anomeric effects) in dihydrodioxins 7 and 8 are of particular interest because the anomeric effect is often associated with substituted saturated heterocycles and is generally defined as a preference of an electronegative substituent for the axial position rather than the equatorial position [eq. (1)].^{9–11} In this connection, hyperconjugative orbital interactions were also found in 1,3-dioxacyclohexane (1,3-dioxane) and 1,4-dioxacyclohexane (1,4-dioxane).⁸

This study was also undertaken to determine the influences of substituting two sulfur atoms for methylene groups in cyclohexene, to calculate the relative stability of the conformers of the dihydrodithiins 1–4, and to examine the possibility of $n_S \rightarrow \sigma_{C-S}^*$, $n_S \rightarrow \sigma_{C-H_{ax}}^*$, $\sigma_{C-S} \rightarrow \sigma_{C-H_{eq}}^*$, and $\sigma_{C-H_{eq}} \rightarrow \sigma_{C-S}^*$ stereoelectronic interactions (anomeric effects) in 1–4. These data are compared with the 6-31G* *ab initio* results for cyclohexane,^{12–14} cyclohexene,^{15–17} and dihydrodioxins 5–8.⁸

Computational Methodology

The energies and optimized geometries for conformers of cyclohexane (Fig. 1),⁸ cyclohexene (Fig. 1),¹⁷ 3,4-dihydro-1,2-dithiin (1), 3,6-dihydro-1,2-dithiin (2),⁴ 4H-1,3-dithiin (3), and 2,3-dihydro-1,4-dithiin (4) were calculated with the SPARTAN 4.0 program using 6-31G* and MP2/6-31G*//6-31G* molecular orbital methods (Figs. 2–7; Tables I–VI).^{4,8,18–28} Frequency calculations were per-

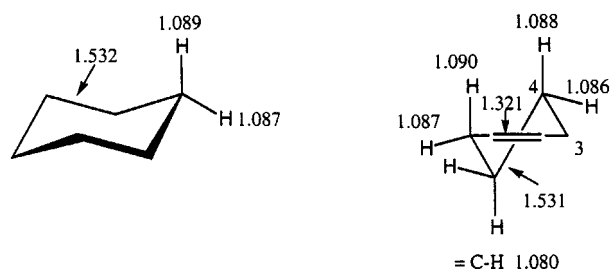
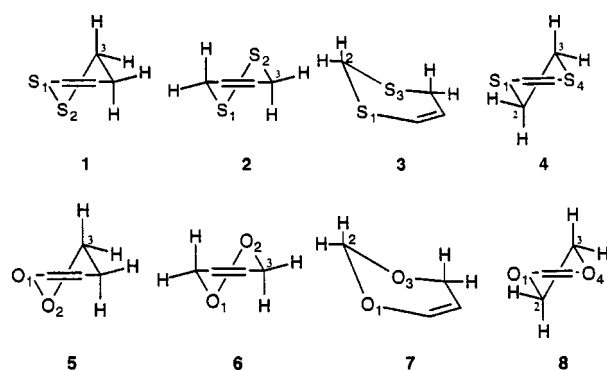


FIGURE 1. Calculated (6-31G*) bond distances (Å) for cyclohexane and cyclohexene.

formed on the 3-21G* and 6-31G* geometry-optimized boat, half-chair, and planar structures of **1**, **2**, **3**, and **4** (Tables VII–X in Supplementary Material).

Twist angles were calculated for the half-chair conformations of **1**–**4** (Fig. 2). In **1** and **2**, the twist angle is the angle formed by the S(1)—S(2) bond and a triangular plane defined by C(3), C(4), and C(6). The twist angle in **3** is formed by the C(2)—S(3) bond and a triangular plane defined by

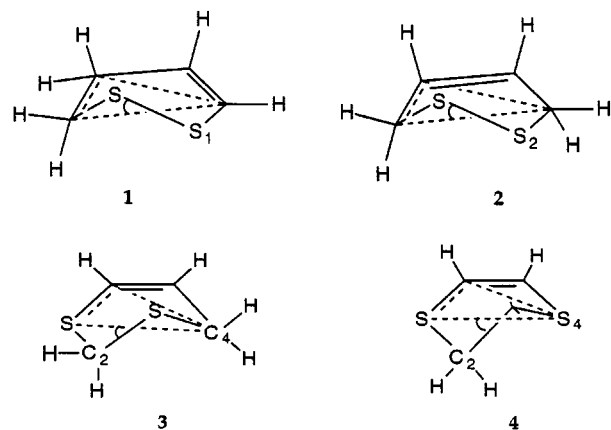


FIGURE 2. Twist angles for 3,4-dihydro-1,2-dithiin (**1**), 3,6-dihydro-1,2-dithiin (**2**), 4H-1,3-dithiin (**3**), and 2,3-dihydro-1,4-dithiin (**4**).

C(4), C(6), and S(1) and the twist angle in **4** is formed by the C(2)—C(3) bond and a triangular plane defined by S(4), C(6), and S(1). The pseudoaxial and pseudoequatorial hydrogens are indicated as H_{pax} and H_{peq}, respectively.

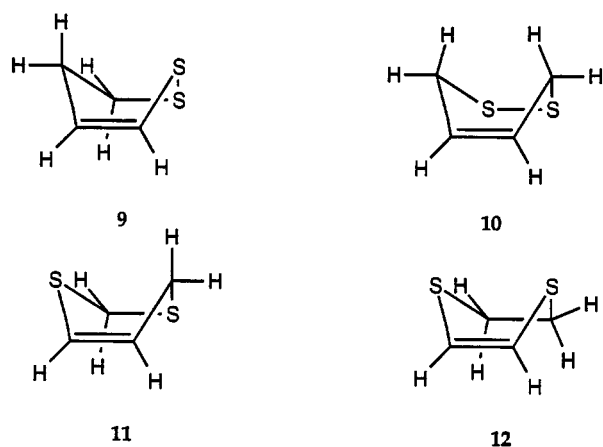
Results and Discussion

3,4-DIHYDRO-1,2-DITHIIN (**1**)

Table I shows the relative energies of the half-chair conformers [**1** (*C*₁, point group), **2** (*C*₂, point group), **3** (*C*₁, point group), and **4** (*C*₂, point group)] of the isomeric dihydrodithiins (Figs. 3–6). At the MP2/6-31G*//6-31G* level, the half-chair conformer of **4** is more stable than those of **1**, **2**, and **3** by 2.5, 3.5, and 3.6 kcal/mol, respectively. The half-chair conformers of **1**, **2**, **3**, and **4** are 2.9, 7.1, 2.0, and 5.6 kcal/mol, respectively, more stable than their boat conformers (Table II, Fig. 7). To alleviate lone pair–lone pair repulsion between the sulfur atoms, **1** adopts the half-chair conformation with a twist angle of 25.8°, which is similar to dihydrodioxin **5** (24.7°) and smaller than the calculated value of 29° for cyclohexene.¹⁷ Twisting of the ring in **1** and **5** reduces both the angle strain and torsional strain by decreasing the inner angles and staggering the methylene groups.

TABLE I. Comparison of the Calculated Energies of Half-Chair Conformers of 3,4-Dihydro-1,2-Dithiin (**1**), 3,6-Dihydro-1,2-Dithiin (**2**), 4H-1,3-Dithiin (**3**), and 2,3-Dihydro-1,4-Dithiin (**4**).

Dihydrodithiin	Half-chair conformer		ΔE = energy difference = $E_4 - E$ (kcal/mol)	
	6-31G*	MP2/6-31G*//6-31G*	6-31G*	MP2/6-31G*//6-31G*
 1	<i>C</i> ₁ –949.963303	<i>C</i> ₁ –950.717485	0.1	2.5
 2	<i>C</i> ₂ –949.963278	<i>C</i> ₂ –950.715792	0.1	3.5
 3	<i>C</i> ₁ –949.959044	<i>C</i> ₁ –950.715619	2.7	3.6
 4	<i>C</i> ₂ –949.963409	<i>C</i> ₂ –950.721409	0.0	0.0



The boat conformer (12) of **4** has one negative frequency (Table X in Supplementary Material [SM]) and is a transition state. The energies of the boat conformers (9–12) of the dihydrodithiins 1–4 are comparable with the exception of structure **10**. The high energy of boat structure **10** may be due to severe lone pair–lone pair repulsion of the S–S atoms. It is 5.3, 5.0, and 5.1 kcal/mol less stable than **9**, **11**, and **12**, respectively. Owing to the constraints of the cyclic system, the torsion angle $\text{=C(6)–S(1)–S(2)–C(3)}$ in **9** is much less than orthogonal.⁵ The $\text{=C(6)–S(1)–S(2)–C(3)}$ torsion angle in **9** is 49.8° (Table III in SM) which indicates that these four atoms are twisted. This twisting reduces the lone pairs interactions of the adjacent sulfur atoms analogous to the preferred gauche conformation adopted by HSSH, which has a nearly orthogonal torsion angle (89.9°). The $\text{C(6)–S(1)–S(2)–C(3)}$ torsion angle in **10** is 0°

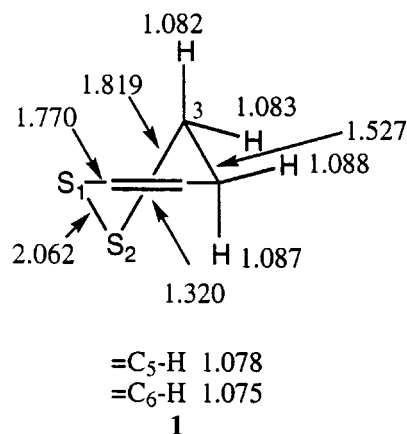


FIGURE 3. Calculated (6-31G*) bond distances (Å) for 3,4-dihydro-1,2-dithiin (**1**).

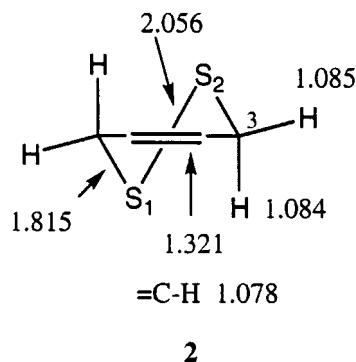


FIGURE 4. Calculated (6-31G*) bond distances (Å) for 3,6-dihydro-1,2-dithiin (**2**).

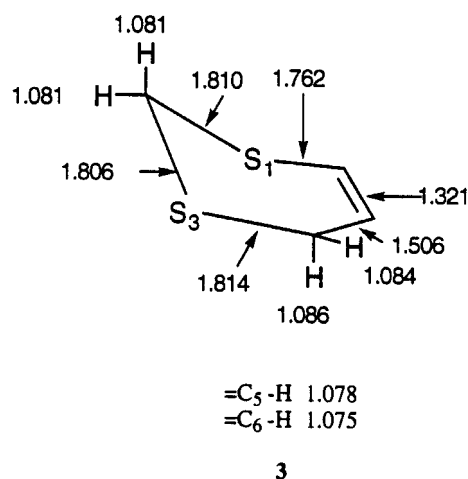


FIGURE 5. Calculated (6-31G*) bond distances (Å) for 4H-1,3-dithiin (**3**).

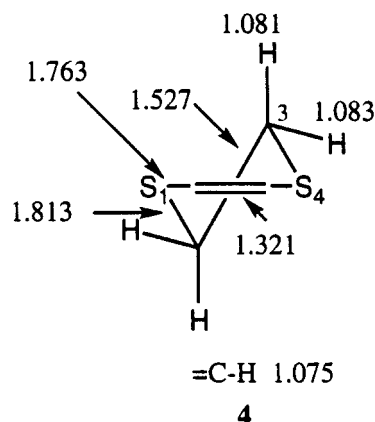


FIGURE 6. Calculated (6-31G*) bond distances (Å) for 2,3-dihydro-1,4-dithiin (**4**).

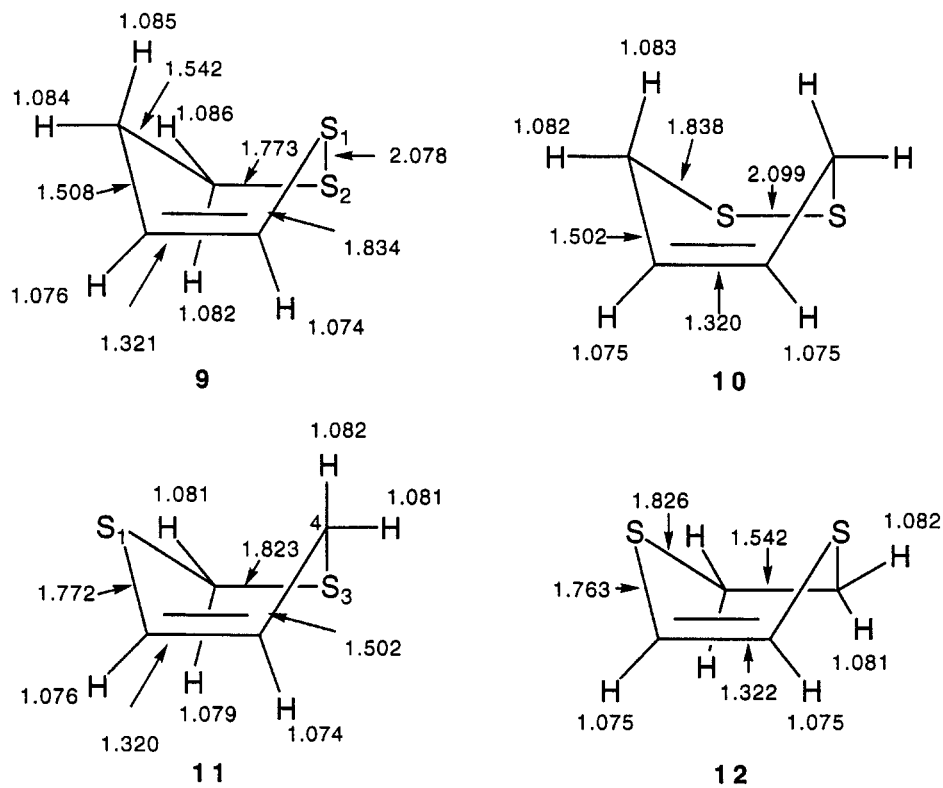


FIGURE 7. Boat conformers (9–12) of 3,4-dihydro-1,2-dithiin (1), 3,6-dihydro-1,2-dithiin (2), 4*H*-1,3-dithiin (3), and 2,3-dihydro-1,4-dithiin (4).

TABLE II. Comparison of Calculated Energies of Boat Conformers of 3,4-Dihydro-1,2-Dithiin (1), 3,6-Dihydro-1,2-Dithiin (2), 4*H*-1,3-Dithiin (3), and 2,3-Dihydro-1,4-Dithiin (4).

Dihydrodithiins	Energy (hartree) boat conformation		ΔE = energy difference = $E_{\text{half-chair}} - E_{\text{boat}}$ (kcal / mol)	
	6-31G*	MP2 / 6-31G* // 6-31G*	6-31G*	MP2 / 6-31G* // 6-31G*
 1	C_1 −949.956983 $\Delta E = 0$	C_1 −950.712914 $\Delta E = 0$	4.0	2.9
 2	C_s −949.950971 $\Delta E = 3.8$	C_s −950.704490 $\Delta E = 5.3$	7.7	7.1
 3	C_1 −949.954400 $\Delta E = 1.6$	C_1 −950.712466 $\Delta E = 0.30$	2.9	2.0
 4	C_1 −949.953267 $\Delta E = 7.3$	C_1 −950.712549 $\Delta E = 0.20$	6.4	5.6

(Table IV in SM), which means these four atoms are coplanar. In **10**, there may be a repulsive transannular nonbonded hydrogen–hydrogen interaction between C(3)—H_{ax} and C(6)—H_{ax}.^{29,30} In structures **11** and **12**, the two sulfur atoms are separated by one and two *sp*³ carbon atoms, respectively, and the lone pairs are not in close proximity. Therefore, they are nearly as stable as **9**. Thus, the relative stability of the boat conformers **9–12** may be due mainly to the structure's ability to lower the sulfur lone pair–lone pair interactions either by twisting along the S—S bond (**9**) or separation of the two sulfur atoms by one or two methylene groups.

The calculated C(3)—S(2), C(6)—S(1), S(1)—S(2), and C(5)=C(6) bond lengths in **1** are 1.819 Å, 1.770 Å, 2.062 Å, and 1.320 Å, respectively (Fig. 3 and Table III in SM). The calculated C=C bond length in cyclohexene is 1.321 Å. In contrast to cyclohexane¹⁴ and cyclohexene (Fig. 1),¹⁷ where the C—H_{ax} bonds are slightly longer than the C—H_{eq} bonds, the C(3)—H_{ax} and C(4)—H_{ax} bonds in **1** are about the same length as the corresponding C—H_{eq} bonds (Fig. 3). The calculated half-chair structure for 3,4-dihydro-1,2-dioxin (**5**) shows that the C(3)—H_{pax} and C(3)—H_{peq} bonds are of comparable length. The C(4)—H_{ax} and C(4)—H_{eq} bonds in **5** are also of comparable length.⁸ In cyclohexene, the C(3)—H_{pax} bond is slightly longer than the C(3)—H_{peq} bond (Fig. 1).¹⁷

The calculated C(3)—S(2)—S(1) and =C(6)—S(1)—S(2) bond angles for the half-chair conformer **1** are 98° and 100.8°, respectively (Table III in SM). Carbon atom 4 and S(1) in **1** lie in the plane of the double bond, where the calculated S(1)—C(6)=C(5)—C(4) torsion angle is 0.2°. The H_{ax}—C(3)—C(4)—H_{ax}, H_{eq}—C(3)—C(4)—H_{eq}, C(3)—C(4)—C(5)=C(6), S(2)—C(3)—C(4)—H_{ax}, S(2)—C(3)—C(4)—H_{eq}, and C(6)—S(1)—S(2)—C(3) torsion angles in the half-chair conformation of **1** are 166.5°, 68.9°, 12.0°, 71.7°, 173.0°, and 48.7°, respectively. The calculated dipole moment for **1** is 2.9 debyes.

3,6-DIHYDRO-1,2-DITHIIN (2)

3,6-Dihydro-1,2-dithiin (**2**) is an unstable compound that polymerizes easily. At the MP2/6-31G*//6-31G* level, the half-chair conformer of **2** is 7.1 kcal/mol more stable than the boat form.⁴ The distance between the axial hydrogens in the boat conformer of **2** is 2.498 Å. Because this is close to twice the van der Waals radius of the hydrogen atom (2 × 1.20 Å), the steric interaction between

these hydrogen atoms would destabilize the boat conformation.^{29,30} Eclipsing interactions are observed in the boat conformer with the C(3)—H and C(4)—H bonds and with the C(6)—H and C(5)—H bonds. Cyclohexene undergoes ring inversion with the boat form as a presumed transition state. The barrier for this process is between 4.2 and 7.9 kcal/mol as computed by molecular mechanics and between 5.5 and 6.6 kcal/mol from *ab initio* calculations.^{14,20,21}

The stability of the half-chair conformer of **2** is attributed to its ability to reduce the *n*_σ–*n*_p lone pair electron repulsion on the vicinal sulfur atoms by twisting to make the lone pair electrons orthogonal to each other. The twist angle in **2** (35.5°) is similar to the one in 3,6-dihydrodioxin (**6**, 37.0°),⁸ but larger than those calculated for **1** (25.8°) and cyclohexene (29.0°).¹⁴ The calculated C(3)—S(2), S(1)—S(2), and C(4)=C(5) bond lengths in **2** are 1.815 Å, 2.056 Å, and 1.321 Å, respectively (Fig. 4; Table IV in SM). In **2**, the C—H_{pax} bond lengths are comparable to the C—H_{peq} bond distances (Fig. 4).

The calculated S(1)—S(2)—C(3) bond angle for the half-chair conformer **2** is 98.5°. Carbon atoms 3 and C(6) in **2** lie in the plane of the double bond with a calculated C(3)—C(4)=C(5)—C(6) torsion angle of 1.0°. Dihydrodithiin **2** has a C(3)—S(2)—S(1)—C(6) torsion angle of 61.9°, which is larger than the corresponding angle in **1** (48.7°), but smaller than the calculated value [C(3)—O(2)—O(1)—C(6)] of 78.4° for the half-chair structure of 3,6-dihydro-1,2-dioxin (**6**).^{4,8} The calculated dipole moment for **2** is 2.7 debyes.

Although it has one pair of adjacent methylene groups and a double bond closer to a sulfur atom, the half-chair conformer of **1** is more stable than the half-chair conformer of **2** by 1.0 kcal/mol at the MP2/6-31G*//6-31G* level. This difference in energy could result from a complex interplay of σ_{C—S} → σ_{C—H_{eq}}* or σ_{C—H_{eq}} → σ_{C—S}* stereoelectronic interactions and structural effects. Although an interaction between the sulfur nonbonded electrons and the π-bond electrons of the double bond is destabilizing, an interaction between the sulfur nonbonded electrons and π* in **1** is expected to be stabilizing.

4H-1,3-DITHIIN (3)

At the MP2/6-31G*//6-31G* level, the half-chair conformer of **3** is 2.0 kcal/mol more stable than boat conformation **11**. The relative stability of the half-chair conformer of **3** is attributed in part to

the absence of lone pair–lone pair repulsion and a decrease in torsional strain owing to an absence of adjacent methylene groups. The half-chair conformation of **3**, in which the sulfur atoms are separated by a methylene group, has a calculated twist angle of 33.2° (Fig. 1) which is larger than the twist angle in 4*H*-1,3-dioxin (**7**, 29.2°). The calculated dipole moment of **3** is 1.9 debyes.

The calculated S(1)—C(2), and C(2)—S(3) and C(5)=C(6) bond lengths in **3** are 1.809 Å, 1.806 Å, and 1.321 Å, respectively (Fig. 5; Table V in SM). In contrast to 4*H*-1,3-dioxin (**7**), in which the C—H_{ax} bonds are longer than the C—H_{eq} bonds, the axial and equatorial C—H bonds in **3** are of comparable length.⁸ Thus, there does not appear to be hyperconjugative orbital interactions in dihydrodithiin **3** as calculated for **7**.⁸ Moreover, presumably as a result of hyperconjugative orbital interactions, **7** is 53.1, 54.6, and 3.4 kcal/mol, respectively, more stable than dihydrodioxins **5**, **6**, and **8**.⁸ In the corresponding sulfur series **1–4**, dihydrodithiin **3** is the least stable. Interestingly, 1,2-dithiane is 2.5 and 0.83 kcal/mol, respectively, more stable than 1,3-dithiane and 1,4-dithiane,¹⁷ and 1,3-dioxane is 50.3 and 5.8 kcal/mol, respectively, more stable than 1,2-dioxane and 1,4-dioxane.⁸ Thus, the 1,3-isomers are the least stable in the sulfur series, but are the most stable in the oxygen series.

The C(2)—S(3)—C(4) and =C(6)—S(1)—C(2) bond angles in **3** are 98.2° and 101.0°, respectively (Table V in SM). The C—S—C (=C—S—C) bond angles in thiacyclohexane (thiane, tetrahydro-2*H*-thiopyran),^{31,32} 1,3-dithiacyclohexane (1,3-dithiane),³³ dimethylsulfide,³⁴ methylthioethene,³⁵ and methylthiobenzene³⁶ are 97.6°, 98.1°, 98.9°, 104.5°, and 105.6°, respectively. Thus, some increase in the C—S—C angle is expected for the unsaturated compounds relative to the C—S—C angles in saturated analogs. The S(1)—C(2)—S(3)—C(4), C(2)—S(3)—C(4)—C(5), S(3)—C(4)—C(5)=C(6), C(4)—C(5)=C(6)—S(1), and C(5)—C(6)—S(1)—C(2) dihedral angles in the half-chair conformer of **3** are 64.8°, 49.7°, 21.8°, 0.9°, and 11.2°, respectively (Table V in SM).

2,3-DIHYDRO-1,4-DITHIIN (**4**)

At the MP2/6-31G*//6-31G* level, the half-chair conformer of **4** is 5.6 kcal/mol more stable than its eclipsed boat form **12**,⁵ which is a transition state (Table X in SM). Presumably, the boat conformation is the transition state for ring inversion of the half-chair conformer of **4**. This barrier to

inversion (5.6 kcal/mol) is smaller than the computed value for dihydrodithiin **2** (7.1 kcal/mol), but is in the calculated range for cyclohexene (5.5–6.6 kcal/mol).^{14,20,21} Among the four isomers **1–4**, the half-chair conformer of **4** is more stable than those of **1**, **2**, and **3** by 2.5, 3.5, and 3.6 kcal/mol, respectively. This may be due to the lower dipole moment of **4**. The dipole moments of **1**, **2**, **3**, and **4** are 2.9, 2.7, 1.9, and 0.8 debyes, respectively. In the gas phase among polar molecules, it is generally found that the conformer with the smaller dipole moment has the lower electrostatic energy and a decreased overall energy.^{37,38}

The calculated twist angle (Fig. 2) of 33.0° for **4** is the same as the calculated value for **3** and larger than the calculated value for 2,3-dihydro-1,4-dioxin (**8**, 29.4°). The calculated S(1)—C(2) and C(5)=C(6) bond lengths in **4** are 1.813 Å and 1.321 Å, respectively (Fig. 6, Table VI in SM). In contrast to 2,3-dihydro-1,4-dioxin (**8**), in which the C—H_{ax} bonds are longer than the C—H_{eq} bonds, the C—H_{ax} and C—H_{eq} bonds in **4** are of comparable length.⁸ Thus, the hyperconjugative orbital interactions calculated for dihydrodioxin **8** are not observed in dihydrodithiin **4**. The =C(6)—S(1)—C(2) angle in **4** is 101.5°, which is close to the value of 101.2° for 4*H*-1,3-dithiin (**3**, *vide supra*). The S(1)—C(6)—C(5)—S(4) torsion angle in **4** is 1.3° and the S(1)—C(2)—C(3)—S(4) torsion angle is 70.3°, which is larger than the value of 65° that was determined from vicinal proton coupling constants.⁶

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